Medical and Pediatric Oncology 29:560–562 (1997)

Chemotherapy for Spinal Cord Astrocytoma

Eric Bouffet, MD,[1]* Didier Amat, MD,[2] Yves Devaux, MD,[1] and Claude Desuzinges, MD[3]

Background. The optimal management of spinal cord astrocytomas remains to be defined, as aggressive surgery and radiotherapy are associated with a high risk of morbidity. The value of chemotherapy has not been assessed.

Procedure. The patient in the present report harbored an infiltrating spinal cord tumor causing paraplegia. A limited biopsy showed a grade II astrocytoma. Following biopsy, the patient received sequential chemotherapy with vincristine and carboplatin.

Results. Full neurological recovery and complete radiologically-confirmed remission were achieved after eight months of treatment. Chemotherapy was discontinued after eleven months due to carboplatin hypersensitivity. No adjuvant radiotherapy was given, and the patient remains in complete remission fourteen months after completion of treatment.

Conclusions. Chemotherapy demonstrates a promising activity and could change the standard practice if its efficacy is confirmed in larger studies. It could be used alone or combined with radiotherapy when post-operative treatment is recommended. Med. Pediatr. Oncol. 29:560–562, 1997.

Key words: astrocytoma; chemotherapy; spinal cord tumor

INTRODUCTION

Primary astrocytomas of the spinal cord account for 6–8% of all primary spinal cord tumors [1]. Since these tumors are rare, reliable information on optimal management is limited and treatment is controversial. Some authors feel that cure may be achieved by complete removal [2]. However, complete removal is often impossible and aggressive surgery increases the potential neurologic morbidity [3–4]. Cord tolerance to radiotherapy is a limiting factor, and optimal radiotherapy must balance the risks of local failure and radiation myelitis [5]. The role of chemotherapy in spinal cord tumors remains poorly defined. However evidence for the response to various agents has been reported in low grade astrocytomas in children. We describe here a promising experience of chemotherapy in an adult patient with spinal cord astrocytoma.

REPORT

A 30-year-old woman without previous medical history developed sudden paraparesia. She presented with a one month history of backpain associated with progressive bilateral lower extremity weakness and paresthesiae. On admission, clinical examination showed a bilateral deficit in the legs with moderate sensory loss. MRI scan at that time showed an heterogeneously enhancing intramedullary tumor extending from C4 to the upper part of D6 (Fig. 1). The patient underwent cervical laminectomy. At surgery the tumor infiltrated the spinal cord, without any cleaved plane with normal tissue. A limited biopsy was performed. Histology was consistent with grade II astrocytoma. Post-operatively the patient received high dose corticosteroids and improved significantly. Due to the significant neurological improvement, a proposal for chemotherapy followed by radiotherapy was adopted. The patient received a ten week course of vincristine and carboplatin as previously described by Packer et al. [6]. She continued to improve neurologically and the steroid dose was progressively decreased and stopped. The MRI assessment following this first course showed a dramatic tumor shrinkage. It was planned to administer a one year chemotherapy program. After five months of treatment, she had returned to preillness status, with a normal life, and was able to walk and even to run. At that time carboplatin doses were lowered by 30%, due to prolonged neutropenia following previous doses. There was no other hematological toxicity and there were no infectious complications. Vincristine doses were decreased by 50% after seven months for

[1]Department of Neuro-Oncology, Centre Léon Bérard, Lyon, France.

[2]Department of Neurosurgery, Hôpital Wertheimer, Lyon, France.

[3]Department of Imaging and Nuclear Medicine, Centre Léon Bérard, Lyon, France.

Institutions where the work has been done: Centre Léon Bérard and Hôpital Wertheimer, Lyon, France.

*Correspondence to: E. Bouffet, Institute of Child Health, Bristol Royal Hospital for Sick Children, St Michael's Hill, Bristol BS2 8BJ, UK.

E-mail: eric.bouffet@bris.ac.uk

Received 6 November 1996; Accepted 6 May 1997

Fig. 1. Post contrast T1 weighted MRI scan demonstrates a large infiltrating spinal tumor with heterogeneous contrast enhancement.

Fig. 2. Post contrast T1 weighted MRI eight months later—loss of contrast enhancement. The pre-operative cervical/dorsal enlargement has disappeared.

progressive neurotoxicity with paresthesiae in both upper and lower extremities. After eight months of treatment the MRI scan showed complete disappearance of all enhancing tumor (Fig. 2). The patient developed an allergic reaction after eleven months and therapy was therefore discontinued. Due to the complete clinical and radiological response, radiotherapy was postponed at the patient's request. No clinical or radiological sign of tumor progression has been observed after a 14 month follow-up period.

DISCUSSION

The initial form of treatment of spinal cord astrocytomas is surgical resection. For some authors, additional radiotherapy is thought more likely to give the best chance of long-term survival [7–11].

Surgical management of spinal cord astrocytomas is however difficult. These tumors are infiltrating, and aggressive attempts to achieve complete removal may cause severe and permanent neurologic damage. The combination of the Cavitron Ultrasonic Surgical Aspirator (CUSA) and laser instrumentation has facilitated surgical excision [3,12]. However, the long-term benefit of extensive surgery has not been demonstrated and recent reports do not support the use of aggressive attempts to remove these lesions [13].

Even when total removal is accomplished there is no doubt that microscopically residual fragments remain. For this reason, many oncologists favor post-operative radiotherapy. There is no convincing evidence that low grade astrocytomas are sensitive to radiotherapy. Although there may be series in which an apparently favorable long-term response to radiotherapy is recorded [7–11], this could be related to the indolent biology of the tumor rather than to the response to radiotherapy. Moreover the optimal dosage of radiotherapy remains unknown. The radiosensitivity of the spinal cord limits the dose of radiation that can be given to the tumor. The most

common doses range from 45–50 Gray, but there is no evidence of a dose response relationship in this tumor. The threshold for radiation injury to tumor-containing spinal cord is encountered at the 50 Gray level using conventional fractionation [14].

The use of chemotherapy in these tumors has rarely been assessed. Chemotherapy has a questionable role in the management of adult astrocytomas [15]. In low grade gliomas, previous experience of chemotherapy has been limited and most of the reports concern infants or children. These studies have been initially conducted in relapsing patients previously irradiated. Lefkovitz et al. described 10 children with recurrent low grade tumors who clinically improved with a chemotherapy regimen associating lomustine and vincristine [16]. However, only one patient had evidence of radiographic improvement. More significant responses have been described using a vincristine and dactinomycin regimen in newly diagnosed children with low grade gliomas [17]. More recent reports described a significant rate of tumor shrinkage using carboplatin alone or in combination with vincristine [6,18]. The largest series has been reported by Packer et al with a 62% response rate in newly diagnosed patients [6]. The majority of the responses occurred in patients with hypothalamic or chiasmatic lesions, but only one child with spinal cord tumor has been treated in this study. The tolerance of the reported regimens is satisfactory. Occasional reductions in the doses of carboplatin or vincristine are necessary for either hematological toxicity or neurotoxicity. Hair loss is mild and often transient. The most critical toxicity is anaphylaxis, occurring in up to 20% of the patients, thought more likely to be carboplatin-related [19]. Although the pediatric experience has given promising results, the length of response to chemotherapy remains unclear. Chemotherapy can arrest the growth of low grade glioma, and thus obviate the need for immediate intervention with radiotherapy. Longer follow-up is required to address long-term control in these pediatric series, and whether chemotherapy can replace radiotherapy in the long-term management, remains uncertain. In spinal cord astrocytomas, many authors do not recommend radiotherapy for patients with low grade tumors thought to have been completely removed. When tumor shrinkage with chemotherapy leads to complete remission as in the present report, there is no obvious reason to recommend adjuvant radiotherapy. The result observed in this patient is promising, but duration of follow-up is short and no conclusion can be drawn from a single report. Further reports or larger studies could help to define the role of chemotherapy as an alternative management of either adult patients or children with low grade astrocytoma of the spine.

REFERENCES

1. Stiller CA, Nectoux J: International incidence of childhood brain and spinal tumours. Int J Epidemiol 23:458–64, 1995.
2. Epstein FJ, Jenkin RD: Spinal cord tumors in children. J Neurosurg 82:516–517, 1995.
3. Cristante L, Herrmann HD, McCormick PC, et al.: Surgical management of intramedullary spinal cord tumors: Functional outcome and sources of morbidity. Neurosurg 35:69–76, 1994.
4. Johnston CE II: Post laminectomy kyphoscoliosis following surgical treatment for spinal cord astrocytoma. Orthopedics 9:587–594, 1986.
5. Marcus RB Jr, Million RR: The incidence of myelitis after irradiation of the cervical spinal cord. Int J Radiat Oncol Biol Phys 19:3–8, 1990.
6. Packer RJ, Lange B, Ater J, et al.: Carboplatin and vincristine for recurrent and newly diagnosed low grade gliomas of childhood. J Clin Oncol 11:850–6, 1993.
7. Chun HC, SchmidtUllrich RK, Wolfson A, et al.: External beam radiotherapy for primary spinal cord tumors. J Neuro Oncol 9: 211–217, 1990.
8. Huddart R, Traish D, Ashley S, et al.: Management of spinal astrocytoma with conservative surgery and radiotherapy. Br J Neurosurg 7:473–81, 1993.
9. OSullivan C, Jenkin RD, Doherty MA, et al.: Spinal cord tumors in children: Long-term results of combined surgical and radiation treatment. J Neurosurg 81:507–512, 1994.
10. Rauhut F, Reinhardt V, Budach V, et al.: Intramedullary pilocytic astrocytomas. A clinical and morphological study after combined surgical and photon or neutron therapy. Neurosurgical Review 12:309–313, 1989.
11. Shirato H, Kamada T, Hida K, et al.: The role of radiotherapy in the management of spinal cord glioma. Int J Radiat Oncol Biol Phys 33:323–328, 1995.
12. Brotchi J, Dewitte O, Levivier M, et al.: A survey of 65 tumors within the spinal cord: surgical results and the importance of preoperative magnetic resonance imaging. Neurosurg 29:651–57, 1991.
13. Minehan KJ, Shaw EG, Scheithauer BW, et al.: Spinal cord astrocytoma: pathological and treatment considerations. J Neurosurg 83:590–5, 1995.
14. McCunniff AJ, Liang MG: Radiation tolerance of the cervical spinal cord. Int J Radiat Oncol Biol Phys 16:675–78, 1989.
15. Lesser GJ, Grossman S: The chemotherapy of high-grade astrocytomas. Sem Oncol 21:220–35, 1994.
16. Lefkowitz IB, Packer RJ, Sutton LN, et al.: Results of the treatment of children with recurrent gliomas with lomustine and vincristine. Cancer 61:896–902, 1988.
17. Packer RJ, Sutton LN, Bilaniuk LT, et al.: Treatment of chiasmatic/hypothalamic gliomas with chemotherapy: an update. Ann Neurol 23:79–85, 1988.
18. Friedman HS, Krisher JP, Burger P, et al.: Treatment of children with progressive or recurrent brain tumors with carboplatin or iproplatin: a Pediatric Oncology Group randomized phase II study. J Clin Oncol 10:249–56, 1992.
19. Chang SM, Fryberger S, Crouse V, et al.: Carboplatin hypersensitivity in children: A report of five patients with brain tumors. Cancer 75:1171–75, 1995.